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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/682,303	10/09/2003	Raul Trillo	ANA 5955 (61834)	7332

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EXAMINER	
JEAN-LOUIS, SAMIRA JM	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
07/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/682,303	TRILLO ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5 and 7-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-5, and 7-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/14/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

This Office Action is in response to the amendment submitted on 04/19/09. Claims 1-2, 4-5, and 7-13 are currently pending in the application. Accordingly, claims 1-2, 4-5, and 7-13 are being examined on the merits herein.

Receipt of the aforementioned claims and remarks is acknowledged and has been entered.

1. Applicant's argument with respect to Saito who teaches halothane administered by inhalation while Gray teaches another route of administration and does not disclose that the aforementioned routes of administration are equivalent in the protective effects against ischemic results has been fully considered. Applicant further argues that the proposed combination of Saito and Gray are impermissible hindsight and that Gray teaches injectable halogenated anesthetics for inducing an anesthetic effect while Saito teaches his halothane agent for maintaining anesthetic effect. Such arguments are not persuasive since Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references. The Examiner respectfully points out that Saito clearly teaches the protective effects of halothane in reducing infarct volume and in preventing transient depolarizations from progressing to terminal depolarizations. While Saito does not

teach parenteral administration, Gray on the other hand teaches parenteral administration of halogenated volatile anesthetic along with an emulsification adjuvant and an emulsifier in a sub-anesthetic amount. While Gray is silent as to the pharmacokinetic differences between inhaled halothane versus injected halothane, Gray indicates that the main reason of the invention is to avoid upsetting children with anesthetic gas containment mask thus suggesting that the pharmacokinetic profiles are equivalent. Moreover, the examiner points out that it is incumbent upon applicant to demonstrate through comparative results that the inhaled halothane is contrastingly unequivalent from injectable halothane given that spurious arguments cannot render a prima facie case unobvious. Finally, Gelb was provided to demonstrate the advantages of subanesthetic amount since administration of subanesthetic amount lead to rousable and coherent patients. As for applicant's arguments that the injectable bolus and infusion was applicable to alpha-choralose and not halothane and did not produce any protective effect, the Examiner contends that it would be obvious for one of ordinary skill in the art to try and administer the anesthetic halothane as a bolus or as infusion with the reasonable expectation that such method of administration will necessarily lead to the same protective effects. Thus, the Examiner contends that Saito in view of Gray and in further Gelb does indeed render obvious applicant's invention.

Applicant's contention that Saito discloses using halothane for maintaining the anesthetic effect while Gray discloses injectable halogenated anesthetics for inducing anesthetic effects has again been fully considered but is not found persuasive. The

Examiner respectfully points out that it is obvious to use the halogenated volatile anesthetic both for inducing and for maintaining an anesthetic effect. In fact, Gray teaches various anesthetic agents including halothane (see Gray, pg. 2, lines 25-27) further supporting the notion that halothane can indeed be used for both inducing and maintaining an anesthetic effect. As for applicant's arguments that one of ordinary skill in the art would not have a reasonable expectation that the subanesthetic amount would lead to a protective effect just like the anesthetic amount in Saito, such arguments are not persuasive as one of ordinary skill in the art would have found it obvious to try the sub-anesthetic amount as taught by Gelb and one of ordinary skill in the art would have indeed had a reasonable expectation of success since Gelb teaches that subanesthetic amounts simply reduce ventilatory responses thereby suggesting protective effects should necessarily be noticed at the lower amount. Again, the Examiner contends that if applicants disagree with the fact that such protective effects do not come about as a result of administering a sub-anesthetic amount, it is incumbent upon them to demonstrate through comparative data that such effects do not actually occur. The Examiner therefore reiterates that the rejection was indeed proper and is therefore maintained.

For the foregoing reasons, the rejection of claims 1-2, 4-5, and 7-13 under 35 U.S.C. § 103 (a) remains proper and is maintained. It is re-stated below for applicant's convenience and is being made Final.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art. 2. Ascertaining the differences between the prior art and the claims at issue. 3. Resolving the level of ordinary skill in the pertinent art. 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 4-5, and 7-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al. (Reduction of Infarct Volume by Halothane: Effect on Cerebral Blood Flow or Perifocal Spreading Depression-Like Depolarizations, Journal of Cerebral Blood Flow and Metabolism, 1997, vol. 17, pp 857-864, previously submitted) in view of Gray et al. (GB2350297, previously submitted) in further view of Gelb et al. (Canad. Anaesth. Soc. J., November 1978, Vol. 25. No. 6, pgs. 488-494, previously submitted).

Saito et al. teach that when halothane was given to cats with induced permanent focal ischemia via left middle cerebral artery occlusion (MCAO), it prevented transient depolarizations from progressing to terminal depolarizations and reduced infarct volumes (see abstract). Thus halothane showed protective properties in studies of experimental brain ischemia (i.e. stroke; instant claims 1, 4-5, and 12). Saito et al. teach on page 2 of 12, that the cats treated with halothane were given halothane before, during and after the MCAO (up to 16 hours; instant claims 7-9; see pg. 2, last paragraph, and pg. 3, first paragraph). Particularly, Saito et al. teach that halothane anesthesia was kept as described throughout the entire experimental protocol suggesting that halothane was administered continuously during the experimental procedure (see pg. 3, first paragraph). Saito et al. also teach that in the α-chloralose

group, a bolus was administered intravenously after preparation of the animals and to keep continuous α-chloralose anesthesia, a continuous infusion was started after the initial bolus was injected (see pg. 3, paragraph 1). Saito et al. further teach, on page 9 of 12, that one explanation of the ameliorative effects of halothane may be due to reduction of ischemia-induced glutamate accumulation similar to that seen with isoflurane. The decreased ischemic glutamate elevation by halothane (or isoflurane) could be responsible for the reduction of SD-like depolarizations and for infarct volume reduction.

Saito et al. do not teach parenteral administration of a halogenated volatile anesthetic, with an emulsification adjuvant and an emulsifier in a sub-anesthetic amount. Similarly, Saito et al. do not teach a bolus or infusion administration of the halogenated volatile.

Saito et al., however, do teach that anesthetic can be administered as an injectable bolus or as an infusion for continuous anesthetic administration.

Gray et al. teach, in the abstract, an injectable anesthetic formulation comprising a halogenated anesthetic compound (such as halothane or isoflurane) and at least one emulsifier (see abstract and pg. 2, lines 22-30). Gray et al. also teach that while most halogenated anesthetics are administered by inhalation, such mode of administration can be relatively slow in some patients and the wearing of a mask for such anesthetics

can be upsetting for some patients and therefore suggest intravenous injections for rapid anesthetic induction effect (see pg.1, lines 8-16). On page 3 of the publication, Gray et al. further teach that the formulations can include an emulsification adjuvant such as soybean oil and an emulsifier such as lecithin. Moreover, additional emulsifiers include polyoxypropylene/polyoxyethylene block co-polymers (see pg. 3, lines 25-30, and pg. 4, lines 1-10). Glycerol may be added as a tonicifier for adjusting the tonicity of the anesthetic formulation to the tonicity of the patient's blood plasma along with pH adjustors and water (see pg. 4, lines 23-30 and pg. 5, lines 1-7).

Gelb et al. teach that it is important for clinical anesthetists to know both the duration of action of drugs and their effects in all concentrations (see pg. 488, left col., paragraph 1). Gelb et al. further teach that general halothane administration can depress the ventilatory response and affect heart rate but sub-anesthetic amounts (i.e. 0.1 MAC or 0.05 MAC; which necessarily reads on applicant's definition of sub-anesthetic amount of halothane as delineated on pg. 4, lines 19-26) result in patients being easily rousable and coherent while symptoms of hypoxaemia are markedly reduced or absent (see pg. 489, left col., paragraph 2, right col., last paragraph and table 1). Importantly, Gelb et al. teach that general anesthetic effect may impair the ventilatory responses but low doses (i.e. sub-anesthetic amount; instant claim 1) markedly reduce such responses (see pg. 493, Summary Section).

Thus, it would have been obvious to one of ordinary skill in the art at the time the

invention was made to utilize the halogenated volatile anesthetic (HVA), halothane, in the method of treating ischemia since Saito et al. teach that halothane and isoflurane (two volatile halogenated anesthetics) have shown protective effects in experimental ischemia. Further it would have been obvious to administer the volatile halogenated anesthetics parenterally as Gray et al. teach that volatile halogenated anesthetics including halothane and isoflurane can be administered in such a manner when using an emulsifier and an emulsifier adjuvant. Likewise, one of ordinary skill in the art would have found it obvious to administer the HVA as a bolus or as an infusion as Saito et al. demonstrated that other anesthetics (i.e. α-chloralose) can be administered in such a way and Gray et al. teach parenteral formulations of halothane or administer the HVA in a sub-anesthetic amount since Gelb et al. teach that low dose halothane administration avoids effects on ventilatory responses.

Regarding the method of treating a heart tissue delineated in claim 13, it is considered obvious for one of ordinary skill in the art to pursue known options within his or her technical grasp. Given that heart and brain tissues can both undergo similar ischemic insults, one of ordinary skill in the art would have been motivated to try halothane in both tissues with a reasonable expectation that halothane will produce similar results in the tissues of the heart.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

07/01/2009

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617